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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/970,020	10/03/2001	Lirong Liu	107223-139 US	8697

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EXAMINER

JOYNES, ROBERT M

ART UNIT PAPER NUMBER

1615

DATE MAILED: 02/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/970,020

Applicant(s)

LIU ET AL.

Examiner

Robert M. Joynes

Art Unit

1615

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-23 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

### DETAILED ACTION

Receipt is acknowledged of applicants' Information Disclosure Statements filed on March 12, 2002 and May 6, 2002.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4, 5, 14, 15 and 21-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

"If the trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of the 35 U.S.C. 112, second paragraph. *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used to properly identify any particular material or product." MPEP 2173.05 (u). The trademark TIMERx, either in the N or the O version, is present in instant claims 4, 5, 14, 15 and 21-23. It is unclear what exactly TIMERx is or what it consists of to fully understand the invention. It is suggested that the claims be amended to reflect the generic name(s) for the recited trademark.

Further, Claim 21 also contains the trademark Prosolv in the controlled release and immediate release compositions. It is unclear what exactly Prosolv is or what it consists of to fully understand the invention. It is suggested that the claims be amended to reflect the generic name(s) for the recited trademark.

Art Unit: 1615

Claim 21 is further unclear because there appears to be a typographical error in the controlled release formulation. It appears that Prosolv was misspelled as Proslov.

Appropriate corrections are suggested.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6-13 and 16-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Gilbert et al. (WO 98/40053). Gilbert teaches a bilayer tablet that has a controlled release and immediate release profile for tramadol (Page 1, lines, 25-31; Page 2, lines 17-37; Page 3, lines 1-3, 30-37; Page 4, lines 1-3, 13-37; Page 5, lines 1-9; Page 6, lines 30-35). The composition is controlled in such a way so as to reduce the adverse side effects of nausea and/or dizziness believed to be associated with the enantiomer (Page 5, lines 3-9). The dosage forms taught by Gilbert may be designed to release either of the enantiomers faster than the other, or before the other (Page 3, lines 30-37; Page 4, lines 1-12). Further the dosage forms can be formulated to deliver the drugs at a constant rate for at least 8 hours preferably 12 hours and most preferably 24 hours (Page 3, lines 30-37). The release profiles taught in the specification and shown in the Figures teach the release profiles of the instant claims. Therefore, Gilbert anticipates all the limitations of Claims 1-3, 6-13 and 16-20.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 6-13 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilbert et al. (WO 98/40053). The teachings of Gilbert are discussed above. Gilbert does not expressly teach the exact ranges recited for the release profiles in the instant claims.

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to prepare a bilayer tablet comprising enantiomers of tramadol wherein the tablet has an immediate release profile and a controlled release profile such that the active agent is released over a 24 hours period. It would also be obvious to vary the ratios of the enantiomers and the drugs to the matrix material in which the drugs are contained.

One of ordinary skill in the art would have been motivated to do this to prepare dosage forms that most effectively deliver the drug such that the adverse side effects associated with the drug are reduced. The ratios would be varied to prepare different release profiles for the tablet formulation to achieve the desired release profile.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 4, 5, 14, 15 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilbert in combination with Baichwal et al. (US 4994276). The teachings of Gilbert are discussed above. Further Gilbert teaches that any conventional controlled-release technology can be used to achieve the desired tablet formulation. Gilbert does not expressly teach the TIMERx formulation.

Baichwal teaches a free-flowing slow-release excipient formulation comprising a heteropolysaccharide (xanthan gum), a polysaccharide (locust bean gum) and an inert filler (Col. 4, lines 7-67). This excipient formulation is used to achieve slow release profiles for various drugs wherein the ratio of the drug to excipient is 1:3-7 and can be varied to achieve dissolution profiles for about 24 hours (Col. 9, lines 3-44). One type of drug that can be release in such a system is an analgesic (Col. 9, line 66 – Col. 10, line 6).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to used the slow release excipient of Baichwal to prepare the controlled release portion of the bilayer tablet of Gilbert. Gilbert teaches any conventional controlled release system can be used to achieve the desired release

Art Unit: 1615

profile for the analgesic tramadol. Baichwal teaches a gum excipient formulation that can be used in combination analgesics that achieves a slow release profile depending on the ratio of drug to excipient used. It would be obvious to vary that ratio to achieve the desired release profile for the composition.

One of ordinary skill in the art would have been motivated to do this to prepare a bilayer tablets in which releases an enantiomer of tramadol over a 24 hours period such that the adverse side effects of the drug are reduced. One would be motivated to use the excipient system of Baichwal for the controlled release portion of the bilayer tablet because of its ability to be used with a wide variety of drugs as well as the inexpensive nature for producing a tablet with such a system.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

### ***Correspondence***


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Joynes whose telephone number is (703) 308-8869. The examiner can normally be reached on Mon.-Thurs. 8:30 - 6:00, alternate Fri. 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3592 for regular communications and (703) 305-3592 for After Final communications.

Art Unit: 1615

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Robert M. Joyner  
Patent Examiner  
Art Unit 1615  
February 10, 2003

  
Gellamudi S. Kishore, PhD  
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